Remarks

Upon entry of the foregoing amendment, claims 6-11 are pending in the application, with claim 6 being the independent claim. Claims 1-5 are cancelled. New claims 10 and 11 are sought to be added.

Support for new claim 10 is found in the specification on page 11, Table A. Support for new claim 11 is found in the specification on page 4, lines 11 and 12. These amendments add no new matter and their entry is respectfully requested.

New Claim 10 is directed to a synergistically effective combination of trifloxystrobin, prothioconazole and tebuconazole at the ratio of 1:0.8:1, which possesses synergism as demonstrated on page 11 of the specification.

New Claim 11 is directed to a method for controlling Pyrenophora or Fusarium by contacting Pyrenophora or Fusarium and/or their habitat with a synergistically effective combination of trifloxystrobin, prothioconazole and tebuconazole. The combination of trifloxystrobin, prothioconazole and tebuconazole possesses synergistic effect for controlling Pyrenophora and Fusarium as demonstrated on page 11 in the specification, and in Examples 1 and 2 in the Declaration by Dr. Peter Dahmen, submitted along with Applicants' Reply of August 22, 2007.

Applicants respectfully submit that new claims 10 and 11 are in condition for allowance.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

I. Description of the Invention

The present invention claims a specific combination comprising fungicidally active compounds trifloxystrobin, prothioconazole and tebuconazole, which possesses a

synergistic effect. Each of claims 6-11 recites a specific ratio for trifloxystrobin: prothioconazole and trifloxystrobin:tebuconazole to achieve the synergistic effect. Claim 11 recites specific fungi to be controlled by the claimed synergistically effective combination.

II. Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 6-9 under 35 U.S.C. § 103(a) as being unpatentable over Isenring et al. (U.S. Patent No. 6,407,100 ("the '100 patent")) and Jautelat et al. (U.S. Patent No. 5,789,430 ("the '430 patent")). Applicants respectfully traverse this rejection.

A. Prima Facie Case of Obviousness Has Not Been Established

Applicants reiterate that for the reasons detailed in Applicants' Replies of May 1, 2006, October 26, 2006, January 29, 2007, August 22, 2007, January 17, 2008, and April 3, 2008, claims 6-9 are not *prima facie* obviousness in view of the cited references.

In sum, taken together, the '100 and '430 patents, at most, teach that fungicidal compounds can and are often combined. However, the present invention is directed to a specific three-compound combination, which comprises trifloxystrobin, prothioconazole and tebuconazole, and possesses a synergistic effect. There is nothing in the cited references that would provide a reason for making the specific three-compound combination of trifloxystrobin, prothioconazole, and tebuconazole, which possesses a synergistic effect.

In addition, in Applicants' Reply of April 3, 2008, Applicants amended claims 6 and 7 to recite specific ratios for the components in the combination. There is nothing in the cited references, would provide a reason for making the synergistic three-

compound combination at the ratios recited in the claims of the present invention. Thus, for this additional reason, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness.

It is noted that, in the outstanding Office Action, the Examiner repeated the rejections made previously without addressing Applicants' amendments to the claims.

B. Synergistic Effect

Even assuming that a *prima facie* case of obviousness is established, the synergistic effect exhibited by the claimed combination is sufficient to overcome a *prima facie* case.

a. Synergistic result presented in the specification

The Examiner stated that "the results presented in the specification on page 11 are not synergistic" and requested Applicants to "explain in detail the synergism." Office Action, pgs 6 and 8.

Applicants reiterate that for the explanations detailed in Applicants' Replies of May 1, 2006, October 26, 2006, January 29, 2007, August 22, 2007, January 17, 2008, and April 3, 2008, the three-compound combination of present invention possesses synergistic effect.

Specifically, according to the Examiner, synergism means "the combined action of two or more agents . . . that is greater than the sum of the action of one of the agents used alone." Office Action, p. 6.

The data on page 11 in the specification shows the claimed combination has a synergistic effect because, when the combination, *e.g.*, trifloxystrobin:prothioconazole:tebuconazole=1:0.85:1, was applied to barley infested by *pyrenophora teres*, the combination has an efficacy of 78%; if each individual

component of the combination, trifloxystrobin, prothioconazole and tebuconazole is applied at the same rate in the combination, each individual component will have an efficacy 23%, 17% and 8%, respectively; and the combined action of the trifloxystrobin, prothioconazole and tebuconazole (78% efficacy) is much greater than the sum of the action of trifloxystrobin, prothioconazole and tebuconazole used alone (23% + 17% + 8% = 48%)[1], thus synergistic according to the Examiner's definition of synergism.

Alternatively, and in addition to the mathematical calculation of synergistic effect presented above, Applicants explained the synergistic effect of the present invention as follows:

The data on page 11 in the specification shows that when acting alone at an application rate of 100 g/ha, each individual component of the combination, trifloxystrobin, prothioconazole and tebuconazole has a percent efficacy of 67%, 56% and 22%, respectively. Therefore, trifloxystrobin with a 67% efficacy is the most potent fungicide in the combination.

While keeping the same application rate of 100 g/ha, but substituting 65 g of the most potent trifloxystrobin (67%) with 30 g of less potent prothioconazole (56%) and 35 g of much less potent tebuconazole (22%), the resulting three-component combination has a percent efficacy of 78%, much greater than that of even the most effective

[1] The data on page 11 in the specification shows that when acting alone at an application rate of 100 g/ha, each individual component of the combination, trifloxystrobin, prothioconazole and tebuconazole has a percent efficacy of 67%, 56% and 22%, respectively. Thus, assuming a linear dose-response correlation, when acting alone at an application rate of 35 g/ha, trifloxystrobin has an expected percent efficacy of 23%; when acting alone at an application rate of 30 g/ha, prothioconazole has an expected percent efficacy of 17%; and when acting alone at an application rate of 35 g/ha, tebuconazole has an expected percent efficacy of 8%. The sum of expected percent efficacy of the three components acting alone at the application rate of 35 g/ha of trifloxystrobin, 30 g/ha of prothioconazole and 35 g/ha of tebuconazole is: 23% + 17% + 8% = 48%.

fungicide trifloxystrobin (67%) used alone at 100 g/ha. The improved efficacy can only be the result of a synergistic effect between the three components because in the absence of a synergistic effect, the resulting three-component combination would be expected to have a percent efficacy less than that of trifloxystrobin (67%) used alone. Therefore, the three-component combination of trifloxystrobin, prothioconazole and tebuconazole as claimed has a synergistic effect.

b. Additional evidence of synergism

(1) Synergism on other phytopathogenic fungi

The Examiner also stated that the data on page 11, Table A in the specification is *Pyrenophora teres* test on barley and "the synergism as claimed cannot be predicated for the effect on any other phytopathogenic fungi". Office Action, p. 6.

Additional results of the claimed combination for other phytopathogenic fungi and on other crops has been provided in the Declaration by Dr. Peter Dahmen, submitted along with Applicants' Replies of August 22, 2007. The examples provided in the Declaration describe *Blumeria graminis* and *Fusarium culmorum* fungi test on wheat. These examples provide further evidence that the claimed combination has synergistic effect in controlling fungi on crops or plants. Therefore, Applicants respectfully submit that the data supports the conclusion that the claimed combination has a synergistic effect in controlling fungi.

(2) Synergism at different ratios

The Examiner further stated that "the data does not commensurate with the scope of claims." Office Action, p. 6.

As stated above, Applicants amended the claim 6 to recite the weight ratio of trifloxystrobin:prothioconazole is from 1:0.1 to 1:10 and the weight ratio of

trifloxystrobin:tebuconazole is from 1:0.1 to 1:10. Applicants also amended the claim 7 to recite the weight ratio of trifloxystrobin:prothioconazole is from 1:0.2 to 1:5 and the weight ratio of trifloxystrobin:tebuconazole is from 1:0.3 to 1:5.

The data on page 11 in the specification demonstrates a synergistic effect of claimed combination at the ratio of trifloxystrobin:prothioconazole:tebuconazole being 1:0.85:1.

Additional data of the claimed combination at other combination ratio has been provided in the Declaration by Dr. Peter Dahmen, submitted along with Applicants' Replies of August 22, 2007. The studies described in Tables 1 and 2 in the Declaration shows the synergistic effect of a combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. These examples provide further evidence that the claimed combination has synergistic effect at a ratio that falls within the claimed range. Therefore, Applicants respectfully submit that the data supports the conclusion that the claimed combination has a synergistic effect.

(3) Data in Dahmen's Declaration

With respect to the data presented in the Declaration by Dr. Peter Dahmen, submitted along with Applicants' Replies of August 22, 2007, the Examiner acknowledged that example 2 "appears to be marginal synergism for *Fusarium culmorum* at the ratio of 1:1:1." However, the Examiner stated that the combination in Example 1 does not indicate synergism for *Blumeria graminis*. Office Action, p. 7. Applicants respectfully traverse.

Applicant reiterate the explanation detailed in Applicants' Replies of August 22, 2007, January 17, 2008, and April 3, 2008, both Example 1 and Example 2 show synergistic effect of the claimed combination.

Specifically, the study described in Table 1 in the Declaration shows the fungicidal effect of a combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. *Blumeria graminis* fungus on wheat was tested. In this study, the wheat plants were first treated with trifloxystrobin, prothioconazole, tebuconazole or a combination of trifloxystrobin, prothioconazole and tebuconazole. Then, *Blumeria graminis* fungus was introduced to the treated wheat plants to test the preventative (protective) effect of the fungicides. As shown in Table 1, when acting alone at an application rate of 3.3 ppm (parts per million), each individual component of the combination, trifloxystrobin, prothioconazole or tebuconazole has a percent efficacy of 63%, 0% and 11%, respectively. According to Colby formula, the calculated percent efficacy of the combination is 67%. However, the observed percent efficacy is 75%, greater than the calculated percent efficacy. Therefore, the combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. has a synergistic effect against *Blumeria graminis* fungus on wheat.

The study described in Table 2 in the Declaration shows the fungicidal effect of a combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. *Fusarium culmorum* fungus on wheat was tested. In this study, the wheat plants were first infested with *Fusarium culmorum* fungus. Then, the infested wheat plants were treated with trifloxystrobin, prothioconazole, tebuconazole or a combination of trifloxystrobin, prothioconazole and tebuconazole to test the curative effect of the fungicides. As shown in Table 2, when acting alone at an application rate of 10 ppm (parts per million), each individual component of the combination, trifloxystrobin, prothioconazole and tebuconazole has a percent efficacy of 29%, 57% and 57%, respectively. For the reasons detailed in Applicants' Supplemental Reply of January 29,

2007, assuming a linear dose-response correlation, when acting alone at an application rate of 3.33 ppm, trifloxystrobin has an expected percent efficacy of 10%[2]; when acting alone at an application rate of 3.33 ppm, prothioconazole has an expected percent efficacy of 19%[3]; and when acting alone at an application rate of 3.33 ppm, tebuconazole has an expected percent efficacy of 19%[4]. The sum of the expected percent efficacy of the three components acting alone at the application rate of 3.33 ppm of trifloxystrobin, 3.33 ppm of prothioconazole and 3.33 ppm of tebuconazole (total application rate of 10 ppm) is 48%[5]. However, at the application rate of 10 ppm of the combination containing 3.33 ppm of trifloxystrobin, 3.33 ppm of prothioconazole and 3.33 ppm of tebuconazole, the combination has an observed efficacy of 71%, much greater than the sum of expected efficacy of 48% of the three components acting alone at the same application rate. Therefore, the combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. has a synergistic effect against *Fusarium culmorum* on wheat.

C. Colby formula

The Examiner questioned the validity of the Colby formula, citing *Ex parte Quadranti*. Office Action, p. 10. Applicants used the Colby formula to illustrate **a** method of calculating an expected efficacy of a given three-component combination. As the Examiner pointed out,

> [t]here is no single, appropriate test for determining whether synergism has been demonstrated for chemical combination; rather, facts show in each case must be analyzed to determine

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[2] 29% x(3.33/10) = 10%

[3] 57% x(3.33/10) = 19%

[4] 57% x(3.33/10) = 19%

[5] 10% + 19% + 19% = 48%

> whether chosen method has clearly and convincingly demonstrated existence of synergism or unobvious result.

Office Action, p. 9. As shown above, Applicants explained the synergistic effect of the claimed invention by using various methods. Applicants do not rely solely on the Colby formula to determine synergism.

D. In re Lemin et al., 408 F.2d 1045; 161 USPQ 288 (1969)

The Examiner cited *In re Lemin et al.*, 161 USPQ 288 for the proposition that in order to show synergism, it is necessary to present data "for each component singly at the total rate applied in combination in addition to the fact that each component must be tested individually at the rate at which it appears in combination." Office Action, p. 11.

As discussed above, with regard to the data on page 11 in the specification, Applicants have shown the expected efficacy of individual components at the rate at which it appears in combination are 23%, 17% and 8% for trifloxystrobin, prothioconazole and tebuconazole respectively.

Furthermore, with regard to the data in Table 2 in the Declaration, Applicants have shown the expected efficacy of individual components at the rate at which it appears in combination are 10%, 19% and 19% for trifloxystrobin, prothioconazole and tebuconazole respectively.

In summary, for the reasons set forth above, and in view of the amendments to claims, Applicants respectfully submit that the data illustrates that the observed efficacy of the three-component combination of trifloxystrobin, prothioconazole and tebuconazole within the recited weight ratios is greater than that of the sum of expected percent efficacy of the three components acting alone and, therefore, is a synergistic

effect. Reconsideration and withdrawal of the outstanding rejection is earnestly solicited.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,
Sterne, Kessler, Goldstein & Fox p.l.l.c.

Lei Zhou
Attorney for Applicants
Registration No. 48,291

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1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

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